

REMARKS/ARGUMENTS

Claims 1-24 and 26-37 are pending.

Claims 1 and 13 have been amended.

Claims 26-37 have been added.

Claim 25 has been cancelled. Thus, the rejection under 35 U.S.C. 112, second paragraph, is no longer applicable.

Support for the amendments is found in the claims and specification, as originally filed. Specifically, claim 13 comprises the limitation of claim 25; claim 26 corresponds to original claim 16; claims 27-25 correspond to original claims 14 and 17-25, respectively; support for claim 36 can be found at page 33, lines 12-13. No new matter is believed to have been added.

The rejection of Claims 13-15, 19-21, and 23-25 under 35 U.S.C. 102(b) over Okada, WO 00/60112, it traversed because while Okada teaches one lipoprotein lipase, the claimed reagent comprises two lipoprotein lipases, one in the first reagent and another in the second reagent (see claim 13 below<sup>1</sup>) that have different activity.

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<sup>1</sup> Claim 13: A reagent for selective measurement of triglycerides contained in very low density lipoprotein and intermediate density lipoprotein or in very low density lipoprotein in a test sample, comprising

a first reagent that comprises: a first selective reaction promoter, which is an ether or ester compound of a polyoxyalkylene capable of reacting lipoprotein lipase selectively with triglycerides contained in low density lipoprotein and high density lipoprotein; a lipoprotein lipase; enzymes which catalyze a series of reactions leading to the generation of hydrogen peroxide or a reduced coenzyme from glycerol; and an enzyme which catalyzes a reaction leading to the conversion of hydrogen peroxide or a reduced coenzyme into another substance, and

a second reagent that comprises a second selective reaction promoter, which is capable of reacting lipoprotein lipase selectively with triglycerides contained in very low density lipoprotein, intermediate density lipoprotein, low density lipoprotein and high density lipoprotein; and a lipoprotein lipase,

wherein the activity of the lipoprotein lipase contained in the first reagent depends on the concentration of a surfactant, while the activity of the lipoprotein lipase contained in the second reagent hardly depends on the concentration of the surfactant.

Okada teaches a reagent for measuring triglycerides in a sample comprising two reagents but only the first reagent comprises a lipoprotein lipase (see page 35, working example 1 of the automated English translation).

Claim 26 corresponds to original claims 16, which was not rejected over Okada.

Thus, Okada does not anticipate the claimed reagent. Applicants request that the rejection be withdrawn.

The rejection of Claims 1-25 under 35 U.S.C. 103(a) over Okada, WO 00/60112, and Matsui, US 6,194,164, is traversed because neither Okada nor Matsui describes a reagent comprising two lipoprotein lipases having different activities related to a surfactant (see claims 13-24 of the present specification) and a reagent comprising two ether or ester compounds of a polyoxyalkylene different in the average mole number of the added polyoxyalkylene in its ether or ester compound, wherein m/n ratio is in the range of 1.1 to 1.2 (see claims 26-37).

The reagent of claim 13 comprises two lipoprotein lipases, wherein the activity of the lipoprotein lipase contained in the first reagent depends on the concentration of a surfactant, while the activity of the lipoprotein lipase contained in the second reagent hardly depends on the concentration of the surfactant.

As described in the present specification, there are have been known methods measuring a cholesterol content in LDL and HDL (page 2).

The reagent of claim 13 has high selectivity to VLDL and IDL and is different from that of Okada. Example 3 shows that using two lipoprotein lipase (dependent and independent upon the concentration of a surfactant) allows measuring triglycerides in VLDL and IDL, while triglycerides contained in the chylomicron fractions, LDL and HDL could hardly be measured (see pages 52-63).

Okada teaches a reagent for measuring triglycerides in a sample comprising two reagents but only the first reagent comprises a lipoprotein lipase (see page 35, working example 1 of the automated English translation).

Matsui describes a reagent for measuring cholesterol in LDL comprising the cholesterol esterase and cholesterol oxidase in the first reagent (col. 2, lines 59-62; tables 1-2 and 4).

Okada and Mitsui do not teach using two different lipoprotein lipases and, therefore, do not make the reagent of claims 13-24 obvious.

The reagent of claims 26 comprises two ether or ester compounds of a polyoxyalkylene different in the average mole number of the added polyoxyalkylene in its ether or ester compound, wherein  $m/n$  ratio is in the range of 1.1 to 1.2, where  $m$  is the average mole number of the added polyoxyalkylene in its ether or ester compound which is used as the first selective reaction promoter and  $n$  is the average mole number of the added polyoxyalkylene in its ether or ester compound which is used as the second selective reaction promoter.

As described in the present specification, the reagent of claim 26 has high selectivity to VLDL and IDL (e.g., pages 43-46). When the average mole number ratio is 1.1-1.2, the triglycerides content in VLDL and IDL can be selectively measured, compared to those contained in chylomicron, LDL, and HDL (page 44, third full paragraph).

Neither Okada nor Mitsui teaches a reagent comprising two ether or ester compounds of a polyoxyalkylene different in the average mole number of the added polyoxyalkylene in its ether or ester compound, wherein  $m/n$  ratio is in the range of 1.1 to 1.2.

The Examiner is of the opinion that it would have been obvious to modify the reagent of Okada and select a particular mole number ratio of the polyoxyalkylene derivatives based upon the teaching of the calculation of HLB values and art-recognized method of using

surfactants with particular HLB values to stabilize specific lipoproteins (pages 7-8 of the Official Action).

However, the methods and reagents of Okada and Matsui are different from each other because they use different enzymes, measure different substance (triglycerides or cholesterol), and exhibit different behaviors towards surfactants such as polyalkylene oxide derivatives.

For example, Okada teaches that BL-9EX (POE(9) lauryl ether) which is a polyalkylene oxide derivative can make an enzyme such as lipoprotein lipase selectively react with triglycerides in LDL and HDL (see page 39, eighth paragraph, of the automated English translation). BL-9EX has HLB value 14.5 (see Annex 1). Mitsui teaches that polyalkylene oxide derivatives having HLB values of not less than 13 and not more than 15 can make cholesterol esterase and cholesterol oxidase selectively react with cholesterol in lipoproteins other than LDL (i.e., HDL, VLDL, CK and the like; col. 3, lines 17-37).

Further, Okada teaches that KF-351 (polyether-modified silicone oil) which is polyalkylene oxide derivative can make an enzyme such as lipoprotein lipase selectively react with triglycerides in IDL and HDL (see page 39, seventh paragraph, of the automated English translation). KF-351 has HLB value of 12 (see Annex 2 and 3). Matsui teaches that polyalkylene oxide derivatives having HLB values of not less than 11 and not more than 13 can make a cholesterol esterase and cholesterol oxidase selectively react with cholesterol in all lipoproteins (i.e., HDL, VLDL, CM, and LDL; col. 4, lines 12-39).

Moreover, Matsui teaches specific method for quantifying cholesterol in LDL using specific surfactants having specific HLB values. Matsui does not teach adjusting HLB values so as surfactants act on different lipoproteins, e.g., IDL and VLDL, not to mention, adjusting a ratio of the average amount of moles of polyoxyalkylene in its ether or ester compound.

Thus, Okada and Matsui do not make claims 26-37 obvious. Applicants request that the rejection be withdrawn.

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.  
Norman F. Oblon



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Marina I. Miller, Ph.D.  
Attorney of Record  
Registration Number 59,091

Customer Number

**22850**

Tel: (703) 413-3000  
Fax: (703) 413 -2220  
(OSMMN 08/07)